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09/990,091	11/21/2001	Joseph M. Fernandez	INVIT1120-3	1288

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EXAMINER
WESSENDORF, TERESA D

ART UNIT	PAPER NUMBER
1639	20

DATE MAILED: 05/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/990,091	Applicant(s) FERNANDEZ ET AL.	
	Examiner T. D. Wessendorf	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47,57,59-63,71-73 and 76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47,57,59-63,71-73 and 76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,15* .
4) ☒ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of Claims

Claims 39-46, 48-56, 58, 64-70, 74-75 and 77-80 have been cancelled in the Amendment of 4/3/03.

Claims 47, 57, 59-63, 71-73 and 76 are under examination.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration by inventor John Heyman (with respect to the date). See 37 CFR 1.52(c).

Specification

The abstract of the disclosure is objected to because of the inclusion of the phraseology "comprising", often used in patent claims. Correction is required. See MPEP § 608.01(b).

The use of the trademark e.g., ZEOCIN, page 9, line 4 has been noted in this application. It should be **capitalized** wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicants are requested to check for other trademarks in the specification since they are too numerous to mention specifically.

The specification is objected to: (1) for failing to update the status of the copending application, S.N. 08/358,344 at page 10, line 22. (2). The sequence [CACCATG] in claim 1 is not contained in any of the sequences in the Sequence Listing.

INCORPORATION OF ESSENTIAL MATERIALS

The attempt to incorporate subject matter into this application by reference to the copending application, cited supra is improper because it is necessary to support the claimed invention. Attention is drawn to MPEP 608.01(p) for the definitions of incorporation of "essential material". The definitions include (1) the material which is necessary to describe the claimed invention and (2) provide an enabling disclosure of the claimed invention. See the last paragraph, second column on page 600-656, REv. 1, Sept. 1995.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or

declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors (typographical, grammatical and idiomatic). Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47, 57, 59-63, 71-73and 76 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification fails to teach how to use the library of expressible gene sequences produced by the claimed method. The disclosure merely teaches a method of making a library of expressible gene sequences. The specification discloses that the library of expressible genes expresses different proteins. It does not positively recite whether this is the use of the library i.e., to express thousands of proteins therefrom. Even assuming that the library would be used for expressing such proteins however, due to the unpredictable effect of the genes, it is highly likely that a particular protein or protein of interest may not be expressed by the recited library. It has been known that the link between expression of the marker protein and the protein of interest can limit the expression of the protein of interest. Equally important, transfected cells expressing too high a level of the marker protein may also not survive. This is because too high a level of the marker protein may interfere with the cell's normal metabolism. Thus,

transformed cells expressing very high levels of the protein of interest may be difficult to obtain because the concomitant high expression of the marker protein may be lethal. Stable, replicatable vectors typically comprise no more than about 20, 000 base pairs, after transfection an enhancer stimulates transcription not only of the gene encoding the protein of interest, but also the gene encoding the marker protein which is used in the isolation of cells which have successfully incorporated the rDNA. Gillies, e.g., col. 1, line 45 up to col. 2, line 5. See also Eckert (Review) e.g., page 17.

Also, the specification fails to teach how to make a library wherein the different claimed enzymes are used to insert a purified and amplified ORFs.

Claims 47, 57, 59-63, 71-73 and 76 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The recited step c of "using an enzyme" to insert the purified amplified ORFs is not supported in the as-filed specification. The specification does not describe how the enzyme is used in said step. Likewise, the recited 5' primer

composing the nucleotide sequences starting CACCATG is not described in the specification (or at least is being inconsistent therewith). The specification, page 14, lines 9-10 recites a template that contains ATG as the start codon and a 5′ primer of Seq. ID. 1. Also, the recited 3′ primer that cause the amplification product to end just prior to a stop codon. This is broadening the specification recitation of the stop codon being at the exact position.

The specification fails to provide a description as to the high-throughput format employed in the method. There is no description in the specification as to what is included or exclude by the format for any high throughput format. Likewise, there is no description that the single 5′ primer will encode the different generic proteins as the enzymes, transcription factors, oncogenes as recited in claim 61. See Strauss (Molecular and Biochemical Parasitology) specifically at page148, col. 2.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 47, 57, 59-63, 71-73 and 76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A). The preamble of claim 71 recites a library that is at odds with the body recitation of a plurality. Furthermore, the preamble recited producing a library. The body of the claims recites selecting transformed cells comprising ORFs. It is not clear within the claimed context, the "orientation" of the ORFs such that a polypeptide is encoded by the ORFs. The term "expressible" connotes uncertainty as to whether said ORF was indeed expressed. "To end just prior to a stop codon" is indefinite as to exactly when the amplification product ends.

B). Claim 76 'suitable' is indefinite as to the vectors or factors and/or conditions considered suitable for the prokaryotic and eukaryotic expression of the vectors.

C). Claim 61 is at odd with the disclosure in reciting a specific primer is required for each expressible gene. This claim recites that the single primer in the base claim will encode the different proteins.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 47, 57, 59-63, 71-73 and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harney (U.S. 6,277,632) in view of Shuman (U.S. 5,766,891) or Ringrose et al (Eur. J. Biochem.)

Harney discloses at col. 1, line 50 up to col. 13,line 18 a method for preparing multicomponent nucleic acid constructs comprising: (a) providing the nucleic acid components and optionally a linking nucleic acid molecule to be assembled into the construct, each nucleic acid component comprising a double stranded nucleic acid molecule having at least one single stranded 5' or 3' terminal sequence, the terminal sequence having sufficient complementarity to either a terminal sequence in a separate nucleic acid component or to a sequence in a linking nucleic acid molecule so as to allow for specific

annealing of complementary sequences and linkage of the components in a predetermined order; (b) incubating the nucleic acid components under conditions which allow for the specific annealing and linkage of the nucleic acid components to thereby produce the nucleic acid multicomponent construct. See the Examples for a detail description of the method and the components used in the method. Harney uses ligase to link the nucleic acid components of the vectors, not vaccinia topoisomerase or integrase/recombinase, as claimed. However, Shuman discloses topoisomerase-based cloning at col. 7,lines 45-67. Shuman discloses that Topoisomerase-based cloning has several advantages over conventional ligase-based cloning of PCR products. First, the topoisomerase procedure circumvents any problems associated with addition of nontemplated nucleotides by DNA polymerase at the 3' end of the amplified DNA. Second, in topoisomerase-mediated cloning, the only molecule that can possibly be ligated is the covalently activated insert and the insert can only be transferred to the vector. There is no potential for in vitro covalent closure of the vector itself, which ensures low background. There is also no opportunity for the inserts to ligate to each other (this can be guaranteed by using 5'-phosphate-terminated PCR primers), which precludes cloning of concatameric repeats. Third, there is no need to

consider the sequence of the DNA being amplified in designing the PCR primers. It is commonplace in standard cloning to introduce a restriction site into the PCR primer and to cleave the PCR products with that restriction enzyme to facilitate joining by ligase to vector.

Ringrose et al discloses at page 911, paragraph bridging col. 1 and col.2 that FLP and Cre have been used extensively in a variety of organisms to engineer specific DNA rearrangement at defined sites. The recombinase system is also useful in that the inverted-repeat target site, like the FLP and Cre, can be read in both orientations without encountering a stop codon, a feature which is necessary if the site is to be placed in an ORF. Accordingly, it would have been obvious to one having ordinary skill in the art to replace the ligase enzyme in the method of Harney with topoisomerase or recombinase as taught by Shuman or Ringrose. One would have been motivated to use topoisomerase or recombinase for the advantages obtained in the used of these enzymes as taught by Shuman and Ringrose.

The indicated allowability of the above claims is regretted and withdrawn in view of the following rejections above.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
April 17, 2003